Pfizer Inc
235 East 42nd Street
New York, NY 10017

Animal Health Group

June 11, 2004

Dr. Lonnie Luther
Staff Chief, Generic Animal Drugs Team (HFV-104)
c/o Division of Dockets Management,
Food and Drug Administration
5630 Fishers Lane, Room 1061 (HFA-305)
Rockville, MD 20852

Re: Suitability Petition, Docket No. 2004P-0175

Dear Dr. Luther:

The purpose of this communication is for Pharmacia & Upjohn (P&U), a division of Pfizer Inc, to provide a response to a suitability petition filed by Intervet Inc. (Docket No. 2004P-0175) on April 14, 2004. In the petition, Intervet requested permission to file an abbreviated new animal drug application (ANADA) for a generic intravaginal progesterone insert for cattle that differs from the pioneer product (EAZI BREED™ CIDR® Cattle Insert; NADA 141-200) in both strength (i.e., concentration) of the active ingredient and potentially both shape and physical characteristics. Intervet Inc. indicates that under Section 512(n)(3) of the Federal Food, Drug, and Cosmetic Act, the proposed ANADA can be filed with limited clinical data, i.e., bioequivalence study.

We disagree with that assumption and request that CVM deny the petition. In the following paragraphs, we provide evidence that a simple bioequivalence study of the lower progesterone concentration (1 gram) in the proposed generic product would be inadequate to prove appropriate efficacy and safety.

1. The suitability petition states that the requirement for efficacy will be met with a bioequivalence study. We disagree that a simple blood level comparison in a relatively small number of animals would be adequate to show efficacy of the generic product. This approach does not address all components of efficacy of intravaginal inserts. A critical component of efficacy is the retention rate. The shape and physical characteristics of vaginal inserts influence retention rate. A true estimate of the retention rate would require studies in hundreds of animals under commercial situations. Furthermore, the labeled uses include

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administration to beef heifers, dairy heifers, beef cows and dairy cows. The size of the vagina and metabolic state varies greatly among these classes of livestock; therefore a study evaluating retention rate in only one of these classes of livestock cannot be used to demonstrate retention in the others. Therefore, the sponsor of this proposed generic intra-vaginal device must be required to demonstrate acceptable retention rates in all the classes of livestock on the product label. The pioneer product demonstrated retention rates greater than 90% in clinical field efficacy studies conducted in beef heifers, dairy heifers, beef cows and dairy cows that utilized hundreds of animals in each class.

2. The author of the suitability petition does not propose to conduct target animal safety studies to support their proposed ANADA. Intervet Inc. does not provide any information on the shape or physical characteristics of the proposed generic product to be able to assess what effect the proposed product may have on the vagina. We believe that an important component of target animal safety for vaginal inserts is the level of vaginal irritation with the use of the product. To support the pioneer product, a target animal safety study was conducted that evaluated the effect of simultaneous administration of up to 3 inserts for a period of 15 days or continuous administration for 45 days on vaginal irritation. Furthermore, vaginal irritation was evaluated in the field efficacy studies that included hundreds of animals, beef heifers, dairy heifers, beef cows and dairy cows. It would therefore be appropriate for the sponsor of the suitability petition to demonstrate target animal safety, in particular, vaginal safety of the proposed generic product.

Given these information, we request that CVM deny the suitability petition. Thank you for your consideration of these concerns.

Sincerely,

Dan T. Domingo, DVM, MAM, ACPV
Associate Director, VMRD-Regulatory Affairs